

specific for a phospholipid, under conditions to form a complex of the purified receptor and said member, wherein said purified receptor is bound to a solid phase,

removing unbound components;

determining the amount of said complex bound to said solid phase;

thereby determining the prethrombotic state; and

comparing the prethrombotic state to prethrombotic values associated with an assortment of diseases and risk factors, thereby diagnosing disease and identifying risk factors.

Please add new claims as follows:

64. The method of claim 36, wherein said purified receptor is bound directly to the solid phase.

65. The method according to claim 36, wherein said purified receptor is bound indirectly to a solid phase.

REMARKS

Claims 36-44 are presently under consideration. Claims 45-63 were withdrawn, without prejudice or disclaimer, pursuant to a Restriction Requirement .

New claims 64 and 65 have been added herewith.

Claims 36-44 were rejected under § 112, second paragraph.

In claim 36, the phrase "wherein said purified receptors bound directly or indirectly to a solid phase" was found objectionable for allegedly not being clear. In amended claim 36, Applicants have deleted the alternative language "directly or

indirectly.” Two new dependent claims, 64 and 65 recite the binding of purified receptors to a solid phase. Claims 36-44 were further objected to for not concluding with the purpose set forth in the preamble. Claim 36 now concludes with, “thereby diagnosing disease and identifying risk factors.” Applicants respectfully submit the claims are in condition for allowance and have been appropriately amended herein.

Claims 36, 37, 39, 40 and 42-44 were rejected under § 102(b) as anticipated by Thiagarajan et al.

Thiagarajan teaches binding purified Annexin V to both resting and agonist-activated platelets or platelet-derived microparticle and then determining the extent of binding by a variety of known methods. However, Applicants’ presently claimed invention features steps not taught by Thiagarajan. Specifically, Thiagarajan fails to teach the step of comparing the prethrombotic state to prethrombotic values associated with an assortment of disease and risk factors.

Claims 36 and 37 were rejected under § 102(b) as anticipated by Rote et al.

Rote teaches binding antiphospholipid antibodies to both resting and activated platelets and determining the binding of antibodies and antigens on the platelets. Applicants respectfully submit that amended claim 36 overcomes this rejection, by adding steps not taught by Rote. For example, Rote fails to teach, “comparing the prethrombotic state to prethrombotic values associated with an assortment of diseases and risk factors.” See claim 36, *supra*.

Since Thiagarajan and Rote fail to teach all the limitations of the presently claimed invention, neither can serve as a proper basis for rejection under § 102.

Applicants, therefore, respectfully request withdrawal of these references as basis for rejection, and allowance of claims 36, 37, 39, 40 and 42-44.

Claims 36-38 and 41 were rejected under § 103(a) over Abrams et al. and Margel et al.; Abrams et al. in view of Rote et al. and Carriere; and Abrams et al. in view of Rote et al. in further view of Hajek and/or Harlow.

The Office Action concedes that Abrams fails to teach antibodies for the detection of phosphatidylserine in activated platelet membranes, use of a solid phase such as particular labels, or alternatives to flow cytometry. Rote et al. allegedly supplies these missing teachings. Margel teaches cell labeling, including both indirect and direct methods. Carriere discloses a method for determining a cell population and this teaching includes platelets. Hajek et al. teaches the agglutination of platelets with a particular antibody coated microsphere population. Harlow et al. teaches agglutination methods.

Although these references teach principles for enabling the presently claimed invention, they fail to teach the application of these principles as presently claimed. It is unclear what would motivate one of ordinary skill in the art to combine these six references to render the presently claimed invention obvious. Even if one were to combine these teachings, none provide for “comparing the prethrombotic state to prethrombotic values associated with an assortment of diseases and risk factors . . .” See claim 36, *supra*.

There is no disclosure or teaching in either Abrams et al., Margel et al. Rote et al., Carriere, Hajek, or Harlow which would suggest the desirability of combining any portions thereof effectively to achieve or suggest Applicants' presently claimed

invention. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Claims 39 and 40 were rejected under § 103(a) as being unpatentable over Abrams et al. in view of Rote et al. and Margel et al in further view of Dachary-Prigent et al.

Dachary-Prigent teaches Annexin V as a probe of aminophospholipid exposure. Please see the Specification on page 14, in the second full paragraph. Dachary-Prigent investigates the activation state of platelets following *in vitro*, i.e. artificial stimulation, whereas one aspect of the method of the present invention microparticles are detected that are generated *in vivo* under real and varied physiological circumstances. This means that the method of Dachary-Prigent is not suitable for the determination of the “real” prethrombotic state of a patient. Therefore, it is unclear what the teachings of Dachary-Prigent add to Abrams, Rote, or Margel, as discussed above. Furthermore, it is unclear what would motivate one of ordinary skill to combine the teachings of Dachary-Prigent with the other prior art of record to achieve or suggest Applicants’ presently claimed invention. Therefore, Applicants respectfully request withdrawal of this rejection and allowance of claims 39 and 40.

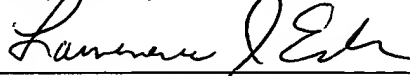
Applicants respectfully submit that this application is now in condition for allowance, and request claims 36-44, 64 and 65 be allowed.

If believed that the application is not in condition for allowance, it is respectfully requested that the undersigned attorney be contacted at the telephone number below.

In the event this response is not considered to be timely filed, Applicants hereby petition for an appropriate extension of time. The fee for this extension may be charged

to our Deposit Account No. 01-2300, along with any other fees which may be required with respect to this application.

Respectfully submitted,



Laurence J. Edson

Registration No. 44,666

ARENT FOX KINTNER PLOTKIN & KAHN, PLLC

1050 Connecticut Avenue, N.W., Suite 600

Washington, D.C. 20036-5339

Tel: (202) 857-6000

Fax: (202) 638-4810

Attachments: Petition for Extension of Time
Marked Up Copy of Claims



MARKED-UP CLAIMS FOR 09/588,553

36. (Amended) A method for determining the prethrombotic state of an individual for the diagnosis of disease and identification of risk factors [an amount or presence of a member selected from the group consisting of circulating microparticles, stimulated procoagulant cells and both circulating microparticles and stimulated procoagulant cells], comprising:

obtaining a body fluid sample comprising a member selected from the group consisting of circulating microparticles, stimulated procoagulant cells and mixtures thereof;

mixing the [a] sample containing said member with a purified receptor [which is] specific for a phospholipid, under conditions to form a complex of the purified receptor and said member, wherein said purified receptor is bound [directly or indirectly] to a solid phase,

removing unbound components;[.]

determining the amount of said complex bound to said solid phase;
thereby determining the prethrombotic state; and

comparing the prethrombotic state to prethrombotic values associated with an assortment of diseases and risk factors, thereby diagnosing disease and identifying risk factors.

64. (New) The method of claim 36, wherein said purified receptor is bound directly to the solid phase.

65. (New) The method according to claim 36, wherein said purified receptor is bound indirectly to a solid phase.